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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/743,618	12/22/2003	Heinz W. Pauls	USAV2002/0262 US NP	7399

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EXAMINER	
COVINGTON, RAYMOND K	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 09/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/743,618	PAULS ET AL.	
	Examiner	Art Unit	
	Raymond Covington	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/28/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-12 and 14-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention: The nature of the invention is the *method of treatment of a patient "subject to" or amelioration* of a disorder or disease selected from a myriad group using compounds of formulae I.

The state of the prior art and predictability: The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. No class of compounds or single compound has been found effective in *of treatment of a patient "subject to" (read* preventing), ameliorating of diseases or disorders. Furthermore, applicant has not demonstrated that the claimed compounds are successful in treating, preventing, ameliorating any of the named diseases or disorders. The diseases or disorders on the list may not be "subject to" (prevention) or amelioration (improvement). The diseases or disorders may be merely treatable. The same would also be true for claim 14 et al with respect to the second compound as one would have to determine which compounds

have the activity of the recited groups and then determine which compounds would provide the desired result.

Guidance and working examples: Compounds according to the invention have been prepared. Applicants have not demonstrated that a single compound according to the invention can prevent, and ameliorate one of the claimed diseases or disorders. Further, many of the diseases or disorders named are in fact a CLASS of disorders or diseases. No single compound or class of compounds is known to treat all the sub-categories of a particular type of disease or disorder. By way of example, applicants name diseases or disorders associated with --- inflammatory reactions, tumor growth, and dermatological condition---. Applicants' are attempting to claim every known associated disease or disorder with the above conditions as well as future diseases and disorders and such is wholly inoperable.

The scope of *treatment of a patient "subject to"* since subject to is merely prevention? Treating and prevention are at odds with one another. Please note that one a subject is being 'treated' for a disease or disorder, the treatment can no longer be 'preventive' in nature. To the extent that *of treatment of a patient "subject to"* is preventing the recurrence of symptom or pathology in a diseased

subject, that is encompassed in the term 'treatment', that is maintenance dose in preventing symptom or pathology from recurrence.

Thus, the specification fails to provide sufficient support of the broad use of the compounds of claim 1 for the *of treatment of a patient "subject to"* or amelioration of any disease. As a result necessitating one of ordinary skill to perform an exhaustive search, for which diseases can be treated, prevented or ameliorated by which compound of claim 1 in order to practice the claimed invention.

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, one of ordinary skill in the art would have to engage in undue experimentation to test which diseases can be treated, prevented, ameliorated by the compounds of the instant claims, with no assurance of success.

It is suggested that claim 4 be amended to delete "subject to a physiological condition" and amelioration, and insert after treating – inhibiting tryptase associated with Mast cell mediated inflammatory conditions- and inserting the limitations of claim 5 drawn to the already identified disease conditions.

Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected as well as enabling disclosure as to how to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention: The nature of the invention is a prodrug of the compounds of formulae I.

The state of the prior art and predictability: The state of the prior art is that there is no absolute predictability even in view of the seemingly high level of skill in the art. It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher,

427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Guidance and working examples: Compounds according to the invention have no been prepared. The specification merely discloses where to find information regarding prod rugs per se.

Undue experimentation would be required because the specification does not disclose what are the specific groups or where the specific groups would be attached.

Thus, the specification fails to provide sufficient support of the broad use of the compounds of claim 1 as prod rugs.

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, one of ordinary skill in the art would have to engage in undue experimentation to test which diseases can be treated, prevented, ameliorated by the compounds of the instant claims, with no assurance of success.

Claims 2, 3, 13 and 23 are rejected as being drawn to a rejected base claim but would be allowed if rewritten in independent form.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-12 and 14-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 10,11 use terms that are confusing and ambiguous. For example, claim 10 - diseases or disorders "related" to atherosclerotic plaque rupture, infarction, stroke or angina. What is meant by these terms? In addition, the intended coverage of scope encompassed those character and conditions that will be correlated in future discovery to be related to the diseases or conditions or disorders so named. The scope of the claims is made even more confusing given the recitation of the myriad of diseases in the claims. The examiner in not merely confused about the scope and meaning of the relatively few terms actually mentioned above but by the totality of the claims.

Further, the scope of 'ameliorating' the above myriad of diseases is also confusing and ambiguous. Please note that ameliorating is merely 'improvement' and as such include both increase and decrease in the effect of the aforementioned diseases or disorders. What constitutes amelioration? Is it that it becomes somewhat better in a patient? Is it less incidents in occurrence? No metes and bounds of the scope of *ameliorating* can be ascertained from the description.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond Covington whose telephone number is (571) 272-0681. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, C. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Raymond Covington
Examiner
Art Unit 1625

RKC

R Desai 9/13/05